Comparison between the Radiographic Findings in Pulmonary Tuberculosis of Children with or without HIV Infection

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Objective: *Identify the difference between radiographic findings in children with pulmonary tuberculosis with and without HIV infection.*
Material and Method: *The authors retrospectively reviewed the chest radiography of 93 children (under 15 years of age) with pulmonary tuberculosis between January 2000 and June 2005. Fifty-two of the children had an HIV co-infection while the remaining 41 children did not. The chest radiographic findings were assessed for parenchymal changes, lymphadenopathy, and pleural effusion.*
Results: *The radiographic manifestations in the HIV-infected group included interstitial infiltration in 39 patients (75%), alveolar infiltration in five patients (9.6%), combined interstitial and alveolar infiltration in seven patients (13.4%), miliary infiltration in one patient (1.9%), and hilar/mediastinal lymphadenopathy in 17 patients (32.6%). One patient had extensive alveolar infiltration in conjunction with multiple cavitatary formations. The findings in the non-HIV-infected group were interstitial infiltration in 30 patients (73.1%), hilar/mediastinal lymphadenopathy in 13 patients (31.7%, 3 of whom had adenopathy without parenchymal infiltration), and pleural effusion in two patients (4.8%). Other less frequent abnormalities included bronchiectasis, peribronchial thickening in the HIV-infected group, and atelectasis and granuloma in the non-HIV-infected group. There was no statistically significant difference in the radiographic findings between the two groups, except the association of hilar/mediastinal lymphadenopathy and pulmonary infiltration. Regarding hilar/mediastinal lymphadenopathy with or without pulmonary infiltration between the two groups, all cases in the HIV-infected group with hilar/mediastinal lymphadenopathy were significantly more associated with pulmonary infiltration (17 patients) than the other group (8 patients) ($p = 0.009$).*
Conclusion: *Hilar/mediastinal lymphadenopathy with pulmonary infiltration strongly suggests the presence of HIV infection in children with pulmonary tuberculosis.*

Keywords: *Pulmonary tuberculosis, Radiographic findings, Children, HIV infection*

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Tuberculosis (TB) persists as an important cause of morbidity and mortality world-wide, mainly as a result of the intractability of the HIV epidemic, and related homelessness, drug abuse and immigration from developing countries[1,2]. An increasing proportion of the global burden of TB is related to HIV, with the highest rate of dual infection occurring in developing countries and children represent one of the high-risk groups in the resurgence of this disease[3]. Children under 5 years of age are at the highest risk for pulmonary TB with rapid progression of the disease[2]. By corollary, HIV is a major risk factor for childhood TB[4].

In 1990, the WHO estimated that there were approximately 1.3 million new cases of TB and approximately 450,000 deaths world-wide from TB in children under 15 years of age[5]. Notwithstanding, to date studies in children have been rare and less conclusive. A major reason is childhood TB is difficult to diagnose reliably, because the signs and symptoms are non-specific and the sputum for direct microscopic examination for acid-fast bacilli is difficult to obtain, especially in very young children.

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The diagnosis of TB in the present study was based on an adapted version of the 1983 WHO guidelines for the diagnosis of pulmonary TB in children[6], when any two of the following were present: (1) complex symptoms suggestive of TB (*i.e.,* fever > 2 weeks, cough > 2 weeks, night sweats and weight loss); (2) household contact with proven TB or symptoms highly suggestive of TB; (3) suggestive chest X-ray (*i.e.,* primary complex, hilar and/or mediastinal lymphadenopathy, cavity, miliary pattern, pleural effusion, any opacity or infiltration not explained by other disease); (4) identification of mycobacteria by acid fast staining for bacilli; (5) positive tuberculin skin test, *i.e.*, an area of induration of 10 mm or more, 48 to 72 hours after injection of 2 tuberculin units of purified protein derivative (PPD RT23; Statens Serum Institute, Copenhagen, Denmark).

To aid in the diagnosis of TB, a variety of scoring systems have been proposed including the tuberculin skin test and chest radiography, both of which were available for all of the presented cases. Regarding chest radiographic features of pulmonary TB in HIV-positive and HIV-negative children, there is sparse literature comparing the difference feature between these groups. The authors' aim was to compare the chest radiographic findings of pulmonary tuberculosis in children with and without HIV infection.

The present study was approved by the Institutional Review Board at Khon Kaen University, Thailand.

Material and Method

This was a retrospective study in which the authors reviewed the chest radiographs and medical records of 93 children who attended between January 2000 and June 2005. The majority of the children were recruited from the Out-Patient Department of Srinagarind Hospital. Some of the patients were referred from other hospitals for diagnosis and treatment. The children who had previously been treated for tuberculosis were excluded.

The medical records of all of the children were analyzed retrospectively for age at presentation, sex, and positive sputum smear or culture for acid fast bacilli (AFB). The radiographs were interpreted by an experienced radiologist in a blinded, retrospective manner and assessed for parenchymal changes, lymphadenopathy, and pleural effusion. The parenchymal changes included pulmonary infiltrate (classified as interstitial, alveolar, combined and miliary infiltrate, cavitation, atelectasis, bronchiectasis, and granuloma).

The diagnosis of pulmonary TB was mainly based upon clinical and radiological features, supplemented by a positive history of contact and a positive tuberculin skin test result.

The Chi square and Fisher exact tests were used to compare proportions between the two groups. $p < 0.05$ was required for statistical significance in the univariate analysis. Stata was the software used.

Results

Ninety-three children (52 boys and 41 girls), between 4 months and 12 years of age (mean, 7.2 years) were included in the present study. Fifty-two children were diagnosed pulmonary tuberculosis with HIV co-infection, while the remaining 41 cases were TB without HIV co-infection. Three children had sputum smear positive for acid fast bacilli, all of whom were non-HIV cases.

The results of the comparison of the chest radiographs between the HIV-infected and non-HIV-infected children with pulmonary TB are shown in Table 1.

The radiographic features in children with HIV infection included interstitial (reticulonodular) infiltraten in 39 patients (75%), alveolar infiltrate in five patients (9.6%), combined infiltrate in seven patients (13.4%), miliary infiltrate in one patient (1.9%), and hilar/mediastinal lymphadenopathy in 17 patients (32.6%) (Fig. 1). One patient had extensive alveolar infiltration in conjunction with multiple cavitary formations (Fig. 2). Pleural effusion was not seen in the HIV-infected group. In the non-HIV-infected children, the radiographic features included

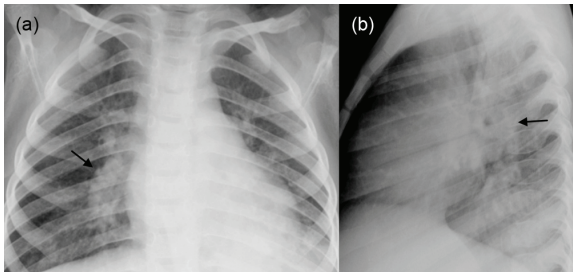

Fig. 1 A 5-year-old boy with pulmonary TB and HIV infection. The posteroanterior (a) and lateral (b) chest radiographs show diffuse reticulonodular infiltrate on both lower lobes and right hilar lymphadenopathy (arrow)

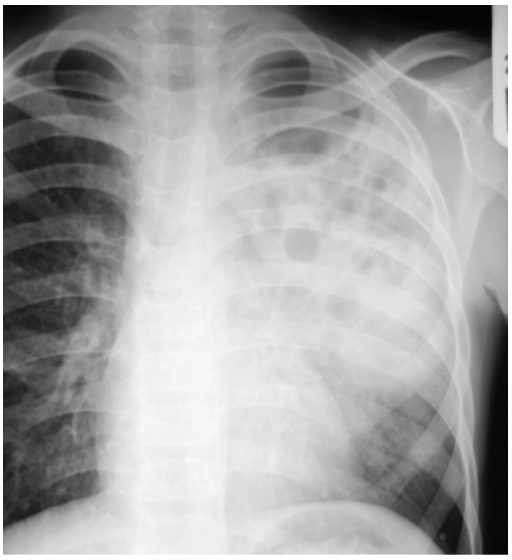

Fig. 2 A 4-year-old boy with pulmonary TB and HIV infection. The posteroanterior chest radiographs reveal extensive consolidation with several small cavitary formations on the left upper lobe and lingular segment. Minimal interstitial infiltration at right perihilar region is also identified

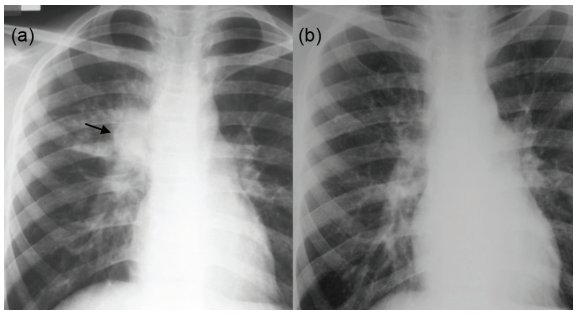

Fig. 3 A 14-year-old boy with pulmonary TB and non-HIV infection. The posteroanterior (a) chest radiograph reveals right hilar lymphadenopathy (arrow) causing partial atelectasis of the right upper lobe. Some reticulonodular infiltration is also noted in right upper lobe. The chest film taken 6 months later after treatment (b) shows near complete resolution of pulmonary lesion and hilar lymphadenopathy

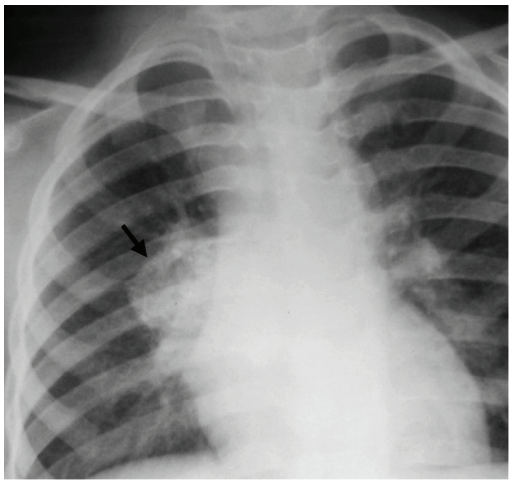

Fig. 4 A 3-year-old boy with pulmonary TB and non-HIV infection. The posteroanterior chest radiograph shows a large, well-defined, soft tissue mass with calcification—thought to be granuloma— locates at superior segment of the right lower lobe (arrow)

interstitial infiltrate in 30 patients (73.1%), alveolar infiltrate in five patients (12.1%), combined infiltrate in three patients (7.3%), cavitation in one patients (2.4%), hilar/mediastinal lymphadenopathy in 13 patients (31.7%), and pleural effusion in two patients (4.8%) (Fig. 3).

The other radiographic features in the HIV-infected group were bronchiectasis (5) and peribronchial thickening (4). The non-HIV-infected group had atelectasis in two patients and right lower lobe mass with calcification in one case (Fig. 4). In both groups, the most common radiographic finding was interstitial infiltration (*viz.,* the reticulonodular type) while the second most common finding was hilar/mediastinal lymphadenopathy.

The comparison of radiographic findings between the two groups indicated that there was no statistically significant difference vis-à-vis pulmonary infiltration, cavity, hilar/mediastinal lymphadenopathy or pleural effusion ($p > 0.05$) (Table 1).

The exception was that all of the cases in the HIV-infected group with hilar/mediastinal lymphadenopathy were associated with pulmonary infiltration (17/17, 100%) compared to 8 of 13 in the non-HIV TB group (61.5%), which was highly statistically significant ($p = 0.009$) (Table 2).

Discussion

Despite being a treatable and preventable disease, tuberculosis is a persistent, major health problem in Thailand. Childhood tuberculosis is a consequence of prolonged close contact with an adult who has sputum positive for *Mycobacterium tuberculosis* (MTB). Notwithstanding, TB in children has a very limited impact on the epidemiological

Table 1. Comparison of chest radiographs between HIV- and non-HIV-infected cases of children with pulmonary TB

Features	No. of subjects (n = 93)		
	HIV infection (n = 52)	Non-HIV infection (n = 41)**	p-value
Infiltration			
Interstitial (reticulonodular)	39 (75%)	30 (73.1%)	NS
Alveolar	5 (9.6%)	5 (12.1%)	NS
Combined (interstitial + alveolar)	7 (13.4%)	3 (7.3%)	NS
Miliary	1 (1.9%)	0	NS
Cavitation	1*	1 (2.4%)	NS
Hilar/mediastinal-lymphadenopathy	17 (32.6%)	13 (31.7%)	NS
Pleural effusion	0	2 (4.8%)	NS

NS = not significant ($p \geq 0.05$)
* Conjunction with alveolar infiltration
** 3 children had sputum smear positive for acid fast bacilli

Table 2. Comparison of hilar/mediastinal lymphadenopathy with and without pulmonary infiltration between HIV- and non-HIV-infected children

Hilar/mediastinal-lymphadenopathy	HIV-infected (n = 17)	Non-HIV-infected (n = 13)	p-value
With infiltration	17 (100%)	8 (61.5%)	0.009
Without infiltration	0	3 (23%)	NS
With atelectasis	0	2 (15.3%)	NS

NS = not significant ($p \geq 0.05$)

situation in a community because of the small number of smear positive cases among children. In Srinagarind Hospital, the diagnosis of childhood TB is based mainly upon clinical and radiological features supplemented by a positive history of contact and a positive tuberculin test result.

Most pulmonary TB cases among infants are primary TB. The primary infection begins with deposition of infected droplets in the lung alveoli, followed by parenchymal inflammation[7,8]. The initial inflammation produces localized alveolar consolidation, which is the primary focus. This may, although rarely, progress to involve a segment or an entire lobe and usually is not visible on chest radiographs[8,9]. The infection then spreads to the central lymph nodes from the primary focus via draining lymphatic vessels (appearing as a linear interstitial pattern on chest radiographs), resulting in regional lymphadenopathy. The primary focus together with the enlarged lymph nodes drain it is called the Ranke complex[8-11].

In most cases, mild parenchymal lesions and lymphadenopathy resolve spontaneously; however, in some cases, especially in young infants, the involved lymph nodes continue to enlarge[7]. Caseating necrosis of the regional lymph nodes progresses and the enlarged nodes may compress the regional bronchi and cause bronchial narrowing, obstruction and emphysema[8,9]. As the disease progresses, inflamed nodes can perforate neighboring bronchus and discharge caseous material into the bronchial tree, causing bronchogenic tuberculosis and focal or lobar pneumonia[12,13]. Hilar/mediastinal lymphadenopathy with or without parenchymal abnormality is the radiographic hallmark of primary childhood TB[8-11,14]. In the present study, hilar/mediastinal lymphadenopathy was a respective 32.6% and 31.7% in HIV- and non-HIV infected children. The most common feature of the pulmonary parenchyma lesion was interstitial infiltration, 75% with HIV infection, and 73.1% without HIV infection. In contrast, in a series of 191 children, Leung et al. reported that hilar/mediastinal lymphadenopathy presented in 175 cases (92%) and was the most common abnormality identified on the initial chest radiographs, particularly in children 0 to 3 years of age[14]. Leung et al also found a lower

prevalence of parenchymal infiltration in the 0- to 3-year-olds (32/63; 51%) compared with the 4- to 15-year-olds (100/128; 78%) ($p < 0.001$). They also identified 130 patients (68%) with parenchymal changes in conjunction with lymphadenopathy and only two cases (1%) had parenchymal involvement in the absence of lymphadenopathy. The reason for the difference from the present study may be that the mean age of the present study was older (*i.e.,* 7.2 years). Also different from Leung et al, Kim et al analyzed 25 non-HIV and non-immuno-compromised children infected by pulmonary tuberculosis. Most of the chest radiographs indicated air space consolidation in conjunction with hilar/mediastinal lymphadenopathy[16]. Isolated lymphadenopathy was rarely seen in their series. By comparison, in the present study, parenchymal lesions were found one-fold more commonly than lymphadenopathy. The overall isolated hilar/mediastinal lymphadenopathy without parenchymal abnormality was rare (3/13 cases in the non-HIV group and none in the HIV group). Pleural effusion in primary TB results from pleural infection via direct extension-rupture of a subpleural lesion into the pleural space or spread from caseous lymphadenopathy or an adjacent spinal lesion[15].

Pleural effusion is not a common feature in primary pulmonary TB in young children and it is rare in infants[14]. The authors found two non-HIV children with pleural effusion (2/93 cases, 2.15%). Mukadi et al reported on radiologic abnormalities found in the TB of 119 children and found no significant differences in the radiologic findings between children with HIV vs. those without HIV[17]. By contrast, Palme et al in a large series of 517 children with TB (58 of whom were HIV-positive) reported pulmonary infiltration was significantly more common in children with HIV[4]. In the present study, the authors found no statistically significant difference in the radiologic findings between the two groups, but when the authors looked for the combination of hilar/mediastinal lymphadenopathy and pulmonary infiltration, there was a significantly higher prevalence in the HIV-infected group than the non-HIV-infected group ($p = 0.009$).

The authors identified two limitations to the present study. First, the authors had a small number of cases in both groups. The number of subjects in the non-HIV-infected group was significantly less than in the HIV-infected group because the majority of non-HIV-infected children were referred to Srinagarind Hospital for diagnosis of pulmonary TB then returned home (with their chest radiographs) for treatment at a nearby regional hospital. The chest radiographs for these cases were therefore not available for review. Second, the lateral chest radiograph was not available in any of the children so the ability to detect hilar/mediastinal lymphadenopathy was not possible since both the AP/PA plus lateral views are needed to detect this.

Although the study had a limited number of subjects for comparing the radiographic findings of pulmonary tuberculosis of children with HIV and non-HIV infection, the authors concluded that a frequent chest radiographic feature of pulmonary tuberculosis in the children included interstitial infiltration (reticulonodular) and hilar/mediastinal lymphadenopathy. There was no statistically significant difference in the radiologic findings between the two groups; however, when the authors combined hilar/mediastinal lymphadenopathy and pulmonary infiltration, there was a significantly higher prevalence in the HIV-infected group than the non-HIV-infected group ($p = 0.009$).

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Potential conflicts of interest

None.

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การเปรียบเทียบระหว่างภาพรังสีของวัณโรคปอดในเด็กที่มีภาวะติดเชื้อและไม่ติดเชื้อเอชไอวี

จิราภรณ์ ศรีนัครินทร์, เนตรดาว รุ่งพิทยานนท์, จามรี ธีรตกุลพิศาล, ภพ โกศลารักษ์, ตุลา เทียนศิริ

วัตถุประสงค์: *เพื่อศึกษาความแตกต่างของลักษณะภาพรังสีปอดในผู้ป่วยเด็กวัณโรคปอดที่ติดเชื้อและไม่ติดเชื้อ เอชไอวี*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังของภาพรังสีปอดของผู้ป่วยวัณโรคเด็กจำนวน 93 ราย (ที่มีอายุน้อยกว่า 15 ปี) ซึ่งประกอบด้วยผู้ป่วยที่ติดเชื้อเอชไอวีจำนวน 52 ราย และไม่พบเชื้อเอชไอวีจำนวน 41 ราย เป็นการศึกษาตั้งแต่เดือนมกราคม ปี พ.ศ. 2543 จนถึง เดือนกรกฎาคม ปี พ.ศ. 2548 ลักษณะภาพรังสีปอดที่นำมาศึกษาประกอบไปด้วย parenchymal infiltration, hilar/mediastinum lymphadenopathy และน้ำในช่องปอด (pleural effusion)*

ผลการศึกษา: *จากการศึกษาพบลักษณะภาพรังสีปอดของวัณโรคในกลุ่มผู้ติดเชื้อเอชไอวีประกอบไปด้วย interstitial infiltration 39 ราย (ร้อยละ 75), alveolar infiltration 5 ราย (ร้อยละ 9.6), interstitial ร่วมกับ alveolar infiltration 7 ราย (ร้อยละ 13.4), miliary infiltration 1 ราย (ร้อยละ 1.9), และ hilar/mediastinal lymphadenopathy 17 ราย (ร้อยละ 32.6) ผู้ติดเชื้อหนึ่งรายที่มี alveolar infiltration พบ cavitation ร่วมด้วย ส่วนลักษณะภาพรังสีปอด ของวัณโรคในกลุ่มผู้ที่ไม่ติดเชื้อเอชไอวีประกอบไปด้วย interstitial infiltration 30 ราย (ร้อยละ 73.1), hilar/mediastinal lymphadenopathy 13 ราย (ร้อยละ 31.7) และน้ำในช่องปอด (pleural effusion) 2 ราย (ร้อยละ 4.8) ลักษณะภาพรังสีปอดทั้งหมดในผู้ป่วยวัณโรคปอดของทั้งสองกลุ่มไม่พบความแตกต่างทางสถิติอย่างมีนัยสำคัญ แต่เมื่อศึกษาภาพรังสีปอดชนิด hilar/mediastinal lymphadenopathy รวมกับ parenchyma infiltration ของทั้งสองกลุ่ม พบว่ากลุ่มผู้ติดเชื้อเอชไอวีมี pulmonary infiltration ร่วมด้วยทุกราย (17 ราย) ซึ่งแตกต่างจากกลุ่มผู้ไม่ติดเชื้อ (8 ราย) อย่างมีนัยสำคัญทางสถิติ ($p = 0.009$)*

สรุป: *การพบลักษณะภาพรังสีปอดชนิด hilar/mediastinal lymphadenopathy ร่วมกับความผิดปกติของเนื้อปอด (pulmonary infiltration) ช่วยชี้แนะว่ามีภาวะการติดเชื้อเอชไอวีในผู้ป่วยเด็กวัณโรคปอด*